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Case Report

Metastatic meningioma: Case report of a WHO grade I meningioma with liver metastases and review of the literature

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ABSTRACT

Meningioma represents the most frequently diagnosed primary brain tumor, accounting for over one-third of central nervous system neoplasms. The majority of tumors are categorized as benign. However, albeit rarely, meningiomas may metastasize to distant sites. We describe a 78-year-old man with a history of recurrent World Health Organization grade I meningioma managed who presented for evaluation of weakness and urinary retention. A computed tomography scan obtained in the emergency department revealed multiple scattered low-density liver lesions. Subsequent magnetic resonance imaging showed a 5.5-centimeter heterogeneous enhancing mass with 2 smaller enhancing lesions suspicious for a primary or secondary malignant neoplasm. Microscopic examination of a tissue sample obtained via liver biopsy demonstrated a metastatic spindle cell neoplasm with histologic features compatible with a diagnosis of World Health Organization grade I transitional meningioma. The patient was referred to hematology/oncology for systemic therapy.

Introduction

Meningiomas are the most common primary brain tumors diagnosed in the United States [1]. Indeed, this typically benign neoplasm is thought to affect nearly 1% of the general population [2]. Tumors are usually asymptomatic and found incidentally on magnetic resonance imaging (MRI). However, patients with large meningiomas may develop neurologic symptoms – most commonly headaches or visual disturbances – due to mass effect [3]. Metastases are extremely rare [4]. A presumptive diagnosis of meningioma is often established via radiologic identification of a homogenous, hemispheric, enhancing extra-axial mass located most frequently in the cerebral convexity, parasagittal, or sphenoid wing regions [5]. Biopsy is required for definitive

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diagnosis. Management typically involves tumor resection and close follow-up. However, individuals with recurrent and/or metastatic disease may benefit from systemic therapy [6].

We describe the clinical and radiologic findings of a 78-year-old man with recurrent meningioma who presented with liver metastases. We also review the radiologic features of meningioma and summarize the differential diagnosis for this condition.

Case report

In 2011, a 71-year-old Asian man presented to his primary care provider for evaluation of right-sided headaches and left-sided weakness. Physical examination was notable for a positive left-sided Babinski sign and palpable right-sided mass beneath the scalp.

A gadolinium-enhanced MRI was performed and revealed an extra-axial mass measuring $6 \times 3 \times 3.5$ centimeters in the occipital region with extracranial extension into the subgaleal space. There was heterogeneous enhancement as well as hemorrhage along the inferior aspect of the mass. Compression and displacement of the adjacent right occipital lobes was noted. The superior sagittal sinus was not well-visualized where the mass extended to the midline, and therefore patency of the superior sagittal sinus could not be confirmed. However, compression and displacement was evident, and right hemispheric subdural hemorrhage and subarachnoid hemorrhage in the parietal sulci was indicative of possible venous sinus invasion (Fig. 1). Right-to-left subfalcine herniation of approximately 4 millimeters was also observed (Fig. 2). A computerized tomography (CT) angiogram and venogram with 3-dimensional (3D) reconstruction was subsequently acquired to evaluate the intracranial vasculature; these studies demonstrated inward displacement of the superior sagittal sinus (Fig. 3). Contrast-enhanced CT imaging of the body was performed to assess for a primary tumor; this showed multiple renal and liver cysts but no evidence of metastatic disease.

Partial resection of the mass was performed 1 month after the patient's initial presentation; complete resection could not be achieved due to involvement of the superior sagittal sinus. Microscopic examination of a tissue specimen collected during surgery showed a neoplasm comprised of epithelioid cells forming fascicular and whorling patterns consistent with a diagnosis of transitional meningioma (World Health Organization [WHO] grade I). Surgery was followed by extensive rehabilitation with gradual resolution of the previously-described neurologic symptoms.

The patient was monitored with brain MRIs every 6 months following neurosurgery. There were no signs of progression until 2013, at which time tumor growth was noted in and around the superior sagittal sinus. The patient subsequently underwent image-guided radiotherapy. Follow-up MRIs performed 1 and 6 months later showed no further growth. Continued surveillance with biannual MRIs was recommended.

Tumor enlargement was once again noted in 2016. Surveillance MRI showed interval enlargement of the posterior parietal extra-axial mass to $4.1 \times 4.1 \times 2.5$ centimeters with involvement of the superior sagittal sinus. Surgical intervention was recommended. However, the patient remained asymptomatic and refused surgery, instead opting for continued monitoring. A repeat MRI in early 2017 showed further interval size increase. Approximately 1 month later, the patient presented to the emergency department with dizziness, word-finding difficulty, and left hemiplegia. MRI showed continued size increase with mass effect on the right posterior horn of the right lateral ventricle. At the level of the tumor, the superior sagittal sinus showed no evidence of flow void, indicating invasion of the sinus (Fig. 4). Subtotal surgical resection was performed 3 weeks later.

The patient received 6 months of adjuvant radiotherapy following surgery and recovered much of his neurologic function. However, follow-up MRI performed in early 2018 once again showed recrudescence of the posterior aspect of the sagittal meningioma. Neuro-oncology recommended salvage chemotherapy and the patient began treatment with bevacizumab.

The patient presented 3 months later with weakness and urinary retention and was found to have severe sepsis with multiorgan dysfunction. A CT scan of the abdomen was obtained to assess for bevacizumab-related gastrointestinal perforation. No acute abdominal pathology was identified. However, multiple scattered hepatic low-density solid lesions were noted. A subsequent MRI of the liver showed a 5.5-centimeter heterogeneous enhancing mass in hepatic segment 7/8 with 2 smaller enhancing lesions superiorly (Fig. 5).

The patient responded to antibiotic treatment for sepsis and received tamsulosin to prevent further benign prostatic hyperplasia-related urinary retention. The liver masses were biopsied 2 months later. Hematoxylin and eosin-stained sections of the tissue samples revealed a metastatic spindle cell neoplasm with features compatible with a diagnosis of meningioma. Notably, the tumor had histologic and immunohistochemical findings identical to those of the samples obtained from the patient's previous neurosurgeries in 2011 and 2017. The patient was diagnosed with metastatic meningioma and referred to hematology/oncology for systemic therapy.

Discussion

Imaging plays a central role in the evaluation of meningioma. Indeed, a CT scan is typically the first diagnostic study to be obtained in the setting of a suspected intracranial mass lesion. On noncontrast CT, meningiomas appear as solitary, well-demarcated isodense or slightly hyperdense masses. Lesions are extra-axial with a broad dural base. Large tumors can cause inward displacement of the cortical grey matter. Rarely, an infiltrative growth pattern over the dura is observed; this is referred to as "meningioma en plaque." Edema is often present, manifesting as a low-density region surrounding the neoplasm. Arterial narrowing may be observed in cases in which the surrounding arteries are encased by the tumor.

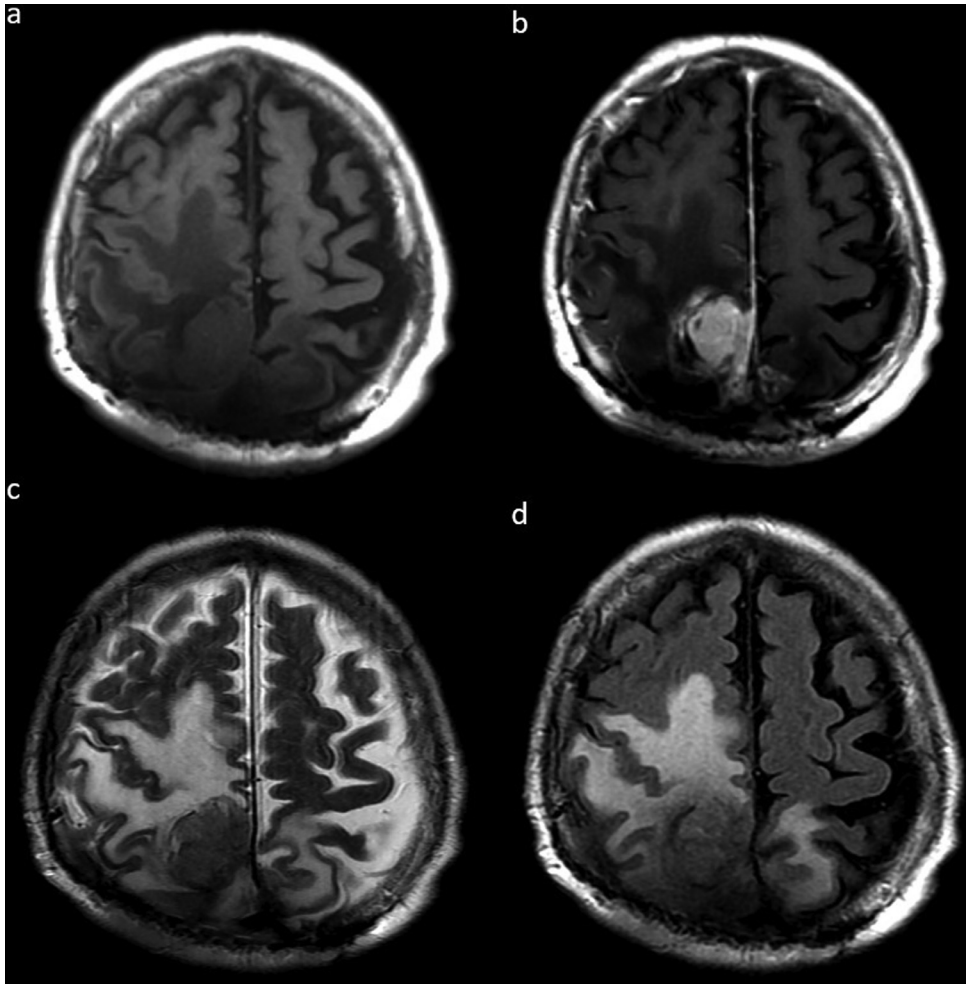

Fig. 1 – (a-d). An MRI was performed with nongadolinium-enhanced T1 (a), gadolinium-enhanced T1 (b), T2 (c), and FLAIR (d) sequences and revealed an extra-axial mass measuring 6 x 3 x 3.5 centimeters in the occipital region with extracranial extension into the subgaleal space. The mass was heterogeneously enhancing. There was heterogenous signal within the calvarium also adjacent to the calavarial defect through which the mass extended extra-cranially. Hemorrhage was present along the inferior aspect of the mass. Compression and displacement of the adjacent right occipital lobes was noted with right hemispheric subdural hemorrhage and subarachnoid hemorrhage in the parietal sulci

Calcifications can be identified in up to 20% of meningiomas and may be inversely correlated with growth potential; thus, robust calcification likely confers a favorable prognosis [7,8]. CT with contrast enhancement typically demonstrates bright and homogenous enhancement. However, atypical meningioma subtypes and densely-calcified neoplasms may exhibit heterogeneous enhancement [5].

MRI represents the gold standard imaging modality for the diagnosis and characterization of meningiomas. Tumors are well-demarcated and may appear isointense or, less commonly, hypointense on T1-weighted sequences. On T2-weighted sequences, meningiomas are typically isointense or hyperintense, but may rarely become hypointense relative to the grey matter. Edema is hypointense on T1-weighted sequences and hyperintense on T2-weighted sequences. Interestingly, some data suggests that the presence of intra-axial edema is predictive of an increased risk of tumor recurrence [9]. Calcifications may also show dephasing on gradient echo or T2 imaging. Tumor invasion into the bone may be observed in some individuals and is characterized by a hypointense signal within the bone seen on T1-weighted sequences; this is due to replacement of the normally hyperintense bone marrow fat with neoplastic cells or hyperostotic bone [7].

T1-weighted MRI with gadolinium-based contrast frequently reveals the “dural tail sign” – a thickening and enhancement of the dura mater in the region adjacent to the tumor that tapers distally, resembling a tail extending from the lesion. The underlying cause of this phenomenon has yet to be established, but it has been hypothesized that it may be the result of reactive hypervascularity and/or tumoral invasion of the dura [10,11]. The presence of the dural tail sign on MRI was once thought to be pathognomonic for meningioma; indeed, it is present in up to 78% of cases [12]. However, this sign has also been associated with glioblastoma multiforme, chloroma, vestibular schwannoma, and other intracranial neoplasms [11].

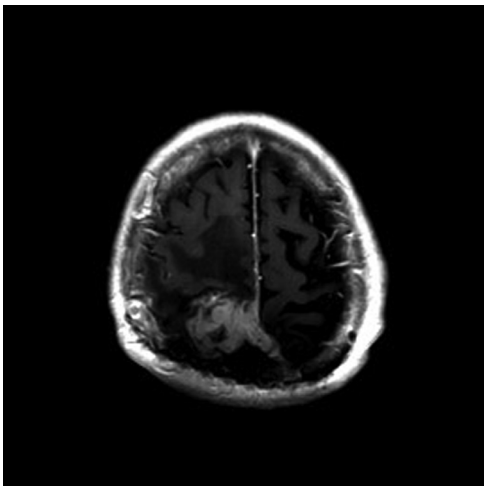

Fig. 2 – A gadolinium-enhanced T1 sequence showed right-to-left subfalcine herniation of approximately 4 millimeters

Histologic subtypes of meningioma may be differentiated based on imaging findings. For instance, a benign secretory meningioma is homogenously enhancing and hyperintense on T2-weighted sequences. In contrast, a malignant anaplastic meningioma may be heterogeneously enhancing and appears mixed hyper- to hypointense on T2-weighted sequences. The distinctive imaging features of each subtype of meningioma are described in a comprehensive 2017 review by Kunimatsu et al [13].

The radiologic features of meningioma may mimic those of other benign and malignant intracranial lesions (Table 1) [14,15]. Therefore, careful correlation of clinical history, physical examination, imaging findings, and/or biopsy results is important in the diagnosis of this common neoplasm.

The clinical presentation of meningioma varies based on the size and location of the tumor. Small meningiomas are extremely common, affecting up to 1% of the general population [2], and are typically asymptomatic. However, mass effect caused by large meningiomas can result in a range of neurologic symptoms. Headaches and visual disturbances are the most common symptoms, affecting approximately 45% and 30% of those with large meningiomas, respectively [3].

Meningiomas most commonly occur in older adults, with a dramatic increase in incidence after the age of 65 years. There is a marked gender predilection, with a female: male ratio of approximately 3:1 in young and middle-aged adults; female predominance is less significant, although still present, in the elderly. Tumors are slightly more common among African Americans as compared to Caucasian and Hispanic individuals. A recent increase in the overall incidence of meningioma has been reported in the literature. However, this may simply reflect improvements in tumor detection and reporting [16].

Metastatic meningioma is rare. The incidence of metastases among all meningiomas is less than 0.2%; even among the aggressive subtypes of WHO grade III tumors, metastases occur in only 40%-45% of patients [4,17]. The route of metastasis has yet to be definitively established. However, hematogenous spread via the paravertebral venous (Batson) plexus appears likely, as 75% of cases of metastatic meningioma occur in individuals with a history of prior surgery or venous sinus invasion [18]. Indeed, our patient presented with significant involvement of the superior sagittal sinus. Other postulated routes of metastasis include the lymphatic system, cerebrospinal fluid, and/or hematogenous dissemination via the jugular vein [19]. The most commonly affected sites of extracranial metastasis are the lungs and the intra-abdominal organs [20].

Our patient presented with a recurrent transitional meningioma (WHO grade I) that metastasized to the liver. To the best of our knowledge, there are only 2 other reported cases of metastatic transitional meningioma in the medical literature: a 45-year-old woman and a 34-year-old man, both of whom presented with multiple pulmonary metastases [21,22].

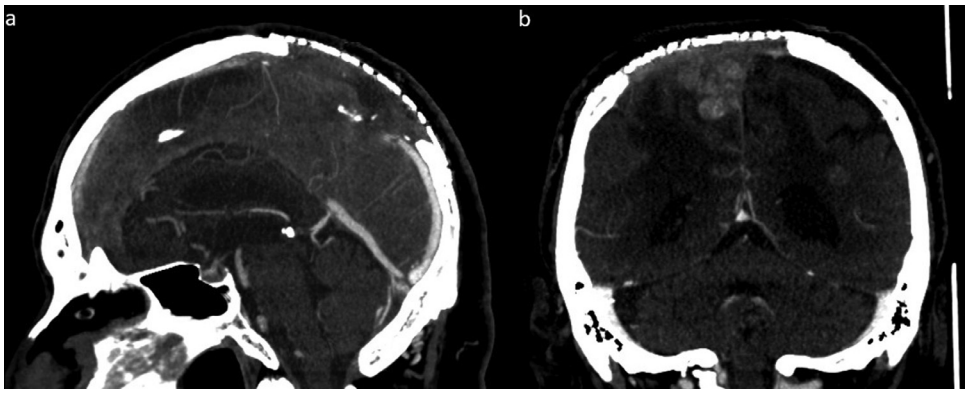

Fig. 3 – (a and b). A CT venogram with 3-dimensional (3D) reconstruction demonstrated inward displacement of the superior sagittal sinus. The extra-axial mass was destroying the posterior parietal bones on both sides of the vertex and extending into the right parietal area. In addition, there was a 3-centimeter area of completely destroyed bone as well as a 5-centimeter area of infiltration in the right parietal bone. A right frontal and parietal thin extra-axial subdural collection was noted. There was an approximately 13-millimeter length of the occluded superior sagittal sinus at the mass

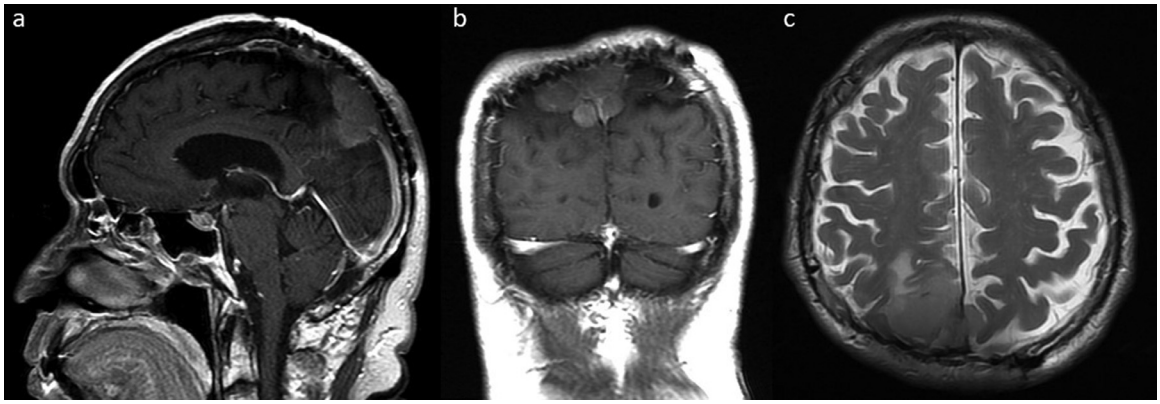

Fig. 4 – (a-c). Gadolinium-enhanced T1-weighted sagittal (a) and coronal (b) views as well as a T2-weighted axial view (c) of an MRI of the brain showed a multilobulated enhancing lesion along the parietal falx extending into the right parasagittal region. Surrounding low T1 signal intensity and high T2 signal intensity was increased since the prior study, representing worsening cerebral edema. There was increased mass effect on the right posterior horn of the right lateral ventricle. The mass at this time measured 3.4 x 4.7 x 5.4 centimeters (on the prior, it had measured 3.7 x 3.2 x 4.2 centimeters). Paracentrally, there was diffusion restriction noted within the tumor. At the level of the tumor, the superior sagittal sinus showed no evidence of flow void; this was strongly suggestive that the tumor had invaded the sagittal sinus

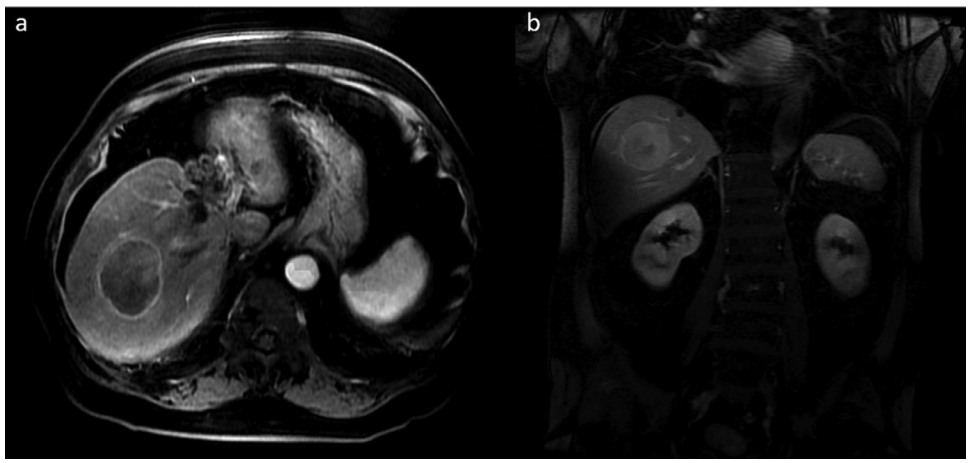

Fig. 5 – (a and b). A contrast-enhanced MRI scan of the body was obtained. T1-weighted axial (a) and coronal (b) views showed a 5.5-centimeter nonenhancing mass in hepatic segment 7/8 with 2 smaller lesions superiorly; these were highly suspicious for a malignant neoplasm

Meningiomas originate from arachnoid cap cells, which normally form the arachnoid villi as well as the outer layer of the arachnoid mater. The mechanism of uncontrolled arachnoid cap cell proliferation has yet to be definitively established. Genetic studies have shown that an inactivation mutation in neurofibromatosis 2 (*NF2*), an important tumor suppressor gene, is implicated in up to 40% of cases of childhood meningioma; some authors suggest that all children presenting with meningioma should be evaluated for neurofibromatosis type 2 [23]. Other genes that have been associated with meningioma include *AKT1, KLF4/TRAF7* (secretory meningioma), and *SMARCB1* (clear cell meningioma). Recent evidence also suggests that overexpression of epidermal growth factor receptor and insulin-like growth factor II (IGF-II) plays a key role in the development of meningioma [24]. However, the complex genetic and molecular mechanisms underlying the development of this neoplasm remain under investigation.

Ionizing radiation represents the most significant risk factor for the development of meningioma, and dental x-rays and radiation therapy for intracranial tumors have been directly linked to meningioma risk. Estrogen and progesterone have also been postulated to contribute to the development of meningioma; indeed, a hormonal pathogenesis may account for the female predilection. However, data concerning the role of estrogen and progesterone in the development of meningioma have been inconsistent. Head trauma, cell phone use, diet, and family history have been hypothesized to contribute

Table 1 – Radiologic differential diagnosis of meningioma [14,15].

Intracranial lesion	Common site(s)	Distinct features on MRI
Gliosarcoma	Temporal lobe	Heterogeneous or cystic appearance with surrounding edema
	Parasagittal region	Heterogeneous, isointense on T1- and T2-weighted sequences
Hemangiopericytoma		Internal vessel voids
		Dural tail sign
Lymphoma	Periventricular white matter	Low apparent diffusion coefficient
	Corpus callosum	Absence of hyperostosis
Meningeal melanocytoma	Meckel cave	Iso- or hyperintense on T1-weighted sequences
	Posterior cranial fossa	Iso- or hypointense on T2-weighted sequences
		Variable enhancement depending on melanin content
Plasma cell granuloma	Fourth ventricle	High signal intensity on T1-weighted sequences
	Hypothalamic region	Low signal intensity on T2-weighted sequences
	Sella	Heterogeneous enhancement
Plasmacytoma	Parietal region	Isointense on T1-weighted sequences
		Iso- or hyperintense on T2-weighted sequences
		Homogenous enhancement
		Often indistinguishable from meningioma

to the development of meningioma, but no data currently exists to support a causative role for any of these theoretical risk factors [16].

Individuals with asymptomatic meningiomas that are not in close proximity to critical structures may elect for observation with serial imaging surveillance [25,26]. However, neurosurgical resection is recommended for all individuals with symptomatic tumors. Adjuvant radiotherapy is advised for patients with WHO grade III meningiomas; the appropriate use of radiotherapy for WHO grade I or II meningiomas remains controversial [24]. Systemic treatment may be considered for recalcitrant meningiomas that recur or progress despite surgery and radiotherapy. Bevacizumab has recently been shown to increase progression-free survival and decrease edema in individuals with meningioma [6]. Vatalanib, a novel tyrosine kinase inhibitor, has also shown promise as a systemic therapy for meningioma [27]. Nevertheless, surgery with or without radiotherapy remains the mainstay of management for this common neoplasm.

Conclusion

Meningioma is the most common intracranial neoplasm diagnosed in the United States. It is usually benign. However, malignant subtypes have been identified. Presumptive diagnosis of meningioma is typically established via CT scan or MRI. On CT scan, tumors appear as well-demarcated extra-axial lesions, often with edema and/or calcifications. The "dural tail sign" – a thickening and enhancement of the dura mater in the region adjacent to the tumor that tapers distally, resembling a tail extending from the lesion – is a classic MRI finding. Definitive diagnosis is established via biopsy. Management of asymptomatic meningiomas may involve surveillance or surgical resection. Fortunately, most individuals have a good prognosis following resection, with an overall survival rate over 80%.

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